REMARKS

Amendments to the Specification and Claims

The specification has been amended to insert a Sequence Listing and appropriate sequence identifiers, as requested by the Office. The Sequence Listing and amendments to the specification contain no new matter in compliance with 37 C.F.R. §1.821(g), as the newly added sequences were disclosed in the specification as originally filed.

The specification has been further amended to refer as Table 2 to the pages containing the structural coordinates of the complex of LXRβ and GW3965 (corresponding to pages 31-71 of WO 2004/058819, published application of parent PCT/IB03/06412) and the complex of LXRβ and T090317 (corresponding to pages 71-357 of WO 2004/058819). Applicants submit that the structural coordinates were set forth in tabular form on pages of the complex of LXRβ and GW3965 and the complex of LXRβ and T090317, although not explicitly labeled as a "Table." The amendment to the specification to refer to Table 2 is purely for matters of form, and does not constitute new matter.

Claims 1-10 and 29-30 have been amended, without prejudice or disclaimer. Claims 11-12, 31-32 and 35 are reiterated. New claims 40-45 have been added. Claims 13-28, 33-34 and 36-39 have been canceled, as these claims are directed to non-elected inventions. Applicants reserve the right to pursue these claims in one or more divisional applications. Upon entry of this amendment, claims 1-12, 29-32, 35 and 40-45 will be pending.

Support for the claim amendments and newly added claims can be found, e.g., in paragraphs [0017-0019], [0125-0126], and Table 1 of US 2007/0060740. No new matter has been added.

The claim amendments and cancellations made herein have been made solely to expedite prosecution of the instant application. Applicants reserve the right to prosecute these claims in other applications.

Sequence Compliance

A new Sequence Listing (in text and paper form) and the above-amendment are believed to satisfy the sequence listing requirements. Applicants hereby state that the contents of the

paper and text format copies of the Sequence Listing submitted herein are identical, and contain no new matter, in accordance with the requirements under 37 C.F.R. 1.821 to 1.825. Thus, the present objection to the Sequence Listing is believed to be obviated.

Claim Objections

On pages 4-5 of the Office Action, the Office has objected to the claims because of certain informalities. Each of the these objections is addressed individually below:

a) Claims 1-4, 6-10, 29 and 30 are objected to because the recitation of "LXRβ." This objection has been obviated by amending claims 1, 8-10, 29 and 30 (as well as claims depending therefrom) to recite in full "Liver X receptor beta," when used for the first time, as suggested by the Office.

b) Claim 7 was objected to because the recitations of "T0901317" and "GW3965," instead of specifying the full chemical name when used for the first time. This objection has been met by providing the full chemical name when the ligands are recited in the claims for the first time (*see e.g.*, claims 1, 30, as amended herein, and newly added claim 40).

c) Claims 9-10 are objected to because the phrase, "LBD." The claims, as amended or newly added herein, specify the phrase "ligand binding domain," instead of "LBD" when used for the first time, thus rendering this objection moot.

d) Claim 9 is objected to because of some missing commas. This objection has been obviated by the amendments to the pending claims.

e) The objection to Claim 10 has been met by inserting the symbol for angstrom (Å) in the claim and correcting the typographical errors pointed out by the Office.

f) Claim 29 is objected to because the recitation of "Leu453", "Trp457" because said recitation is missing a conjunction between "Leu453" and "Trp457." Claim 29 (and newly added claim 30) now recite the conjunction "and" between these residues, thus rendering this objection moot.

e) As to Claim 31, Applicants submit that the sequence of SEQ ID NO:2, which contains amino acid residues Gly213-Glu461 of SEQ ID NO:1, was a non-elected species. Upon allowance of the elected species of SEQ ID NO:1, this sequence should be searched.

In view of the amendments and arguments made herein, the claim objections are now

moot. Reconsideration and withdrawal of the claim objections is respectfully requested.

Rejection of Claims 1-12, 29, 30 and 35 under 35 U.S.C. §112, Second Paragraph

On pages 5-6 of the Office Action, the Office has rejected claims 1-12, 29, 30 and 35 as allegedly being indefinite under 35 U.S.C. §112, second paragraph. Each aspect of this rejection is addressed individually below.

a) Claims 1-3, 8-10, 29 and 30 (4-7, 11, 12 and 35 dependent therefrom) were rejected because the Office considered the phrase, "LXRβ ligand binding domain" or "LBD," to be allegedly unclear and indefinite.

This rejection has been met by amending the rejected claims to either refer to explicitly to an LXRβ ligand binding domain that contains the amino acid sequence from Leu220 to Glu461 of SEQ ID NO:1 (or a sequence highly homologous thereto) (*see e.g.*, claims 1-7 and 35, as amended herein), or to specify the structural coordinates of the amino acid residues set forth in Table 2 (*see e.g.*, claims 29-30).

With respect to claims 8-10, the specification clearly teaches that residues 220 to 461 of human LXRβ as shown in Figure 5 are included in the LXRβ ligand binding domain. A construct corresponding to about the same residues (*i.e.*, spanning Gly213 to Glu461 of human LXRβ) was used for generating the crystals having the space group and unit cell parameters specified by the claims (*see e.g.*, paragraph [0121] of US 2007/0060740.

Thus, Applicants submit that the boundaries of the LXRβ ligand binding domain are either explicitly recited by the claims as amended herein, or understood from the teachings in the specification.

b) Claim 7 was rejected as allegedly being indefinite by the recitation of the phrase, "the internal "LXRβ binding cavity." Without prejudice or disclaimer, this rejection has been met by the amendments to claim 7 made herein.

c) Claim 2 was rejected as allegedly being indefinite by the recitation of the phrase "an amino acid sequence having at least 95% identity with the sequence and which encodes for LXRβ ligand binding domain." This rejection has been met by amending claim 2 to delete this phrase. The pending claims that provide for at least 95% sequence identity to a reference amino acid sequence have been amended to specify that the polypeptide includes the amino acid

sequence specified and has the binding activity recited by the claims. Thus, none of the pending claims recite the phrase objected to by the Office.

d) Claim 29 has been rejected as being allegedly unclear in the recitation of the phrase, "the coordinate tables." Applicants submit that although not explicitly labeled as a "Table," the structural coordinates of the complex of LXRβ and GW3965 were set forth in tabular form on pages 31-71 of WO 2004/058819, and structural coordinates of the complex of LXRβ and T090317 were set forth in tabular form on pages 71-357 of WO 2004/058819. For ease of reference, the specification has been amended to refer to pages 31-357 as "Table 2." Such recitation is merely formalistic to facilitate making reference to the coordinates of this complex and should not constitute new matter.

In view of the amendments and arguments made herein, the rejection of the claims are now obviated. Reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. §112, second paragraph is respectfully requested.

Rejection of Claims 1-12, 29, 30, 32 and 35 under 35 U.S.C. § 112, First Paragraph

Written Description

On pages 6-10 of the outstanding Office Action, the Office has rejected claims 1-12, 29, 30, 32 and 35 under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the written description requirement. To support this rejection, the Office states that:

> The specification discloses only two representative species of the genera of claimed crystals, comprising X-ray diffraction quality crystal of human liver X receptor beta consisting of the contiguous amino acid residues 220 to 461 of SEQ 1D NO: 1 complexed with GW3965, and T0901317, wherein said the crystal has the space group symmetry $P2_12_12_1$ and having the unit cell dimensions a = 59 +/- 3 A. b = 100 +/- 5 A. c = 176 +/- 3 A. a=β =y=90°, or alternatively has the space group P6122 and having the unit cell dimensions a = 59 +/- 3 A b = 59 +/- 3 A c = 294 +/- 3 A= B =90°, y=120° that diffracts x-rays to a resolution of less than or equal to 3 angstroms. Other than these disclosed species, the specification fails to describe any additional representative species of the recited genera, which encompasses any crystals (including crystals that do not diffract X-rays at appreciable resolution for the structural characterization) comprising any 150 or more contiguous or non-contiguous amino acid residues of any LXR β ligand binding domain, optionally complexed with any ligand, wherein said crystal can have widely variant space groups, unit cell dimensions and α, β, and γ angles, optionally

wherein said crystal may produce any structural coordinates upon X-ray diffraction pattern analysis. (Office Action, paragraph bridging pages 8-9).

While Applicants do not concede to any aspect of the Office's stated reasons for rejection, this rejection has been met by amending the claims to: (i) recite the space group and the particular amino acid sequence from Leu220 to Glu461 of SEQ ID NO:1 (or sequences related thereto); (ii) recite the space group and unit cell dimensions of the crystals disclosed in the instant application; and/or (ii) to specify selected or full structural coordinates of the binding pocket of the complexes of LXR β LBD according to the Table disclosed in the specification. Thus, the claims, as amended herein, provide sufficient structural and functional features in common with the crystal structures of LXR β LBD in complex with GW3965, T0901317 or its coactivator peptide (NR box 1 of TIF2) to satisfy the written description requirement, as described in more detail herein.

More specifically, claims 1-7, 35 and newly added claims 40-42, as currently amending, are directed to crystals of LXR β ligand binding domain (and further forming a complex including GW3965, T0901317 or NR box 1 of TIF2) having the space group specified (*e.g.*, $P2_12_12_1$ or $P6_122$) that consist essentially of, or include, the amino acid from Leu220 to Glu461 of human LXR β LBD (SEQ ID NO:1), or a polypeptide having a sequence highly homologous thereto that has the ability to bind selected LXR β ligands. Dependent claims 4-5, 7 and 42 further specify the unit cell parameters of the claimed crystals.

Unlike the Office's characterization that only two representative structures of the claimed crystals were disclosed, the specification actually discloses two sets of crystals for the complex of LXR β LBD and T0901317 having space groups $P2_12_12_1$ and $P6_122$ (*see* specification at paragraph [0125] of US 07/0060740); one crystal structure of the complex of LXR β LBD and GW9365 having space group $P6_122$ (*see* specification at Table 1); and one crystal structure of the complex of LXR β LBD and NR box 1 of TIF2 having space group $P2_12_12_1$ (*see* specification at paragraph [0020] of US 07/0060740). Therefore, four representative crystal structures LXR β LBD in three different complexes with space groups either $P2_12_12_1$ or $P6_122$ were disclosed in the instant specification, as opposed to "only two representative species," as alleged by the Office. Furthermore, the genus of LXR β LBD encompassed by the claims does not have substantial variation, since all of the amino acid sequences must encode a polypeptide having an

amino acid sequence identical or highly similar to a reference sequence. Lastly, the claims have been amended to specify the particular ligands and cofactors complexed with the LXR β LBD, as presently claimed by claims 3, 6, 10 and 40, thus rendering moot the Office's comments as applied to claim 6. In light of the disclosure, the skilled artisan would have concluded at the time of filing of the present application that Applicants were in possession of the common attributes necessary to encompass the members of the claims genus.

Applicants point out to the Office that claims 4-5, 7-10 and 42, as amended herein, are almost identical in scope to hypothetical claim 1 exemplified in case 4 of the "Trilateral Project WM4 Comparative Study on Protein 3-Dimensional (3-D) Structure Related Claims" released in November 2002 ("Trilateral Report"). The USPTO indicated in the Trilateral Report that hypothetical claim 1 would meet the written description requirement because the crystal structure is provided in the claim by specifying the cell unit dimension. More specifically, claim 1 in case 4 of the Trilateral Report is directed to a crystalline form of a known protein, P, and reads as follows: "A crystalline form of protein P having unit cell dimensions of a=4.0nm. b=7.8nm, and c=11.0nm." At pages 8 and 66 of the report, the hypothetical specification of case 4 is described as including, *inter alia*, that the inventors have newly produced a stable crystalline form of protein P and that the description gives experimental data with explanations of how to make the crystals. The Trilateral Report, at page 67, and referring to the claim of case 4, states that "the claim complies with the written description requirement because of the structure of protein P is provided."

Like the hypothetical claim 1 presented in case 4 of the Trilateral Report, claims 4-5, 7-10 and 42, as amended herein, are directed to the crystalline form of a specific known protein (*i.e.*, LXRβ LBD), which was known and characterized in the art prior to the filing date in terms of its structure and function. Also similar to the hypothetical claim 1 presented in case 4, the instant claims recite the unit cell dimensions of the crystal. The present specification discloses, *inter alia*, that the inventors had newly produced at least four crystalline forms of LXRβ LBD, provided LXRβ LBD sequence information, experimental data with explanations on how to make the crystals, and the three dimensional structures of at least two crystalline complexes of LXRβ LBD (see Tables 1 and 2). Thus, Applicants respectfully submit that for at least the

reasons above, the specification amply provides written description support for the crystals of LXRβ LBD as presently set forth in claims 4-5, 7-10 and 42.

As to claim 29 (and claim 30) as amended herein, the Office states that "the genus of claimed crystallized molecules or molecular complexes is drawn to "any structure" because the structure of the crystallized molecules or molecular complexes are only limited by two or more structure coordinates from structure coordinates of any homologue of said molecule or molecular complex wherein said homologue has a root mean square deviation form the backbone atoms of said amino acids of not more than 1.5 A (italicized for added emphasis)."

While Applicants do not concede to any aspect of the Office's stated reasons for rejection, this aspect of the rejection has been met by amending claim 29 (as well as claims 30, 43-45, as presently pending) to specify that the molecular complexes include the full structural coordinates or selected residues (*i.e.*, Ser242, Phe268, Phe271, Thr272, Leu274, Ala275, Ser278, Ile309, Met312, Leu313, Glu315, Thr316, Arg319, Ile327, Phe329, Leu330, Tyr335, Phe340, Leu345, Phe349, Ile350, Ile353, Phe354, His435, Gln438, Va1439, Leu442, Leu449, Leu453, and Trp457), of the binding pocket of the complex LXRβ LBD and either of GW3965 or T0901317, according to the Table disclosed in the specification on pages 31-357 of WO 2004/058819, or a structural deviation of no more than 1.5 Å.

Accordingly, withdrawal of this rejection is respectfully requested.

Enablement

On pages 10-19 of the Office Action, the Office has rejected claims 1-12, 29, 30, 32 and 35 under 35 U.S.C. 112, first paragraph allegedly:

> [B]ecause the specification, while being enabling for a crystal, comprising X-ray diffraction quality crystal of human liver X receptor beta consisting of the contiguous amino acid residues 220 to 461 of SEQ 1D NO: 1 complexed with GW3965, and T0901317, wherein said the crystal has the space group symmetry P212121 and having the unit cell dimensions a = 59 +/-3 A b = 100 +/- 5 A c = 176 +/- 3 A a=b=y=90°, or alternatively has the space group P6122 and having the unit cell dimensions a = 59 +/- 3 A b = 59 +/- 3 A c = 294 +/- 3 A a=90°, y=120° that diffracts x-rays to a resolution of less than or equal to 3 angstroms, does not reasonably provide enablement for (A) any crystal comprising at least 150 amino acid residues of the LXR ligand binding domain; (B) any crystal of LXR LBD belonging to the space group P212121 and having the unit

cell dimensions a = 59 +/- 3 A b = 100 +/- 5 A c.= 176 +/- 3 A a= y =900; (C) any crystal of LXR LBD belonging to the space group P6122 and having the unit cell dimensions a = 59 +/- 3 A b = 59 +/- 3 At = 294 +/- 3 A, a=_=90°, y=120o; (D) any crystal of LXR LBO in complex with a coactivator peptide (TIF2 NR-box 1) belonging .to the space group P21212 and having the unit cell dimensions a = 89 +/- 3 A b = 91 +/- 3 A c = 131 +/- 3 A a=_=y=90o; (E) any crystallized molecule or molecular complex comprising a binding pocket defined by the structure coordinates of human LXR/3 ligand binding domain amino acid residues Ser242, Phe268, Phe271 , Thr272, Leu274, Ala275, Ser278, lle309, Met312, Leu_13. Glu315, Thr316, Arg319. lle327, Phe329, Leu330, Tyr335, Phe340. Leu345, Phe349, lle350, lle353, Phe354, His435, Gln438, Va1439, Leu442, Leu449, Leu453, Trp457, according to the coordinate tables or a homologue of said molecule or molecular complex wherein said homologue has a root mean square deviation form the backbone atoms of said amino acids of not more than 1.5A; and (F) any crystallized composition comprising at least 150 amino acid residues of the LXRβ ligand-binding domain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. (Office Action, pages 10-11).

This rejection has been met by the amendments to claims 1-7, 11-12, 29-30, 32 and 35, and is traversed as applied to claims 8-10. The claims, as currently pending, are directed to crystals of LXRβ ligand binding domain (and further forming a complex including GW3965, T0901317 or NR box 1 of TIF2): (i) having specific space groups (*e.g.*, $P2_12_12_1$ or $P6_122$) and specific amino acids of human LXR β LBD (SEQ ID NO:1) (*e.g.*, Leu-220 to Glu-461 or Gly213 to Glu461); (ii) having the space group and unit cell dimensions of the crystals disclosed in the instant application; or (iii) having the specific structural coordinates of the binding pocket of the complexes of LXR β LBD according to the Tables disclosed in the specification. The genus of LXR β LBD encompassed by the claims does not have substantial variation, since all of the amino acid sequences must encode a polypeptide having an amino acid sequence identical or highly similar to a reference sequence. As described in more detail below, the breadth of the claims, as amended herein, is commensurate in scope with the teachings in the specification.

The present specification describes how to successfully make crystals of several complexes of LXRβ LBD, such as two sets of crystals for the complex of LXR β LBD and T0901317 having space groups $P2_12_12_1$ and $P6_122$ (*see* specification at paragraph [0125] of US 07/0060740); one crystal structure of the complex of LXR β LBD and GW9365 having space group $P6_122$ (*see* specification at Table 1); and one crystal structure of the complex of LXR β LBD and NR box 1 of TIF2 having space group $P2_12_12_1$ (*see* specification at paragraph [0020] of

US 07/0060740). Once the crystallization conditions are established, one of ordinary skilled in the art could have practiced the claimed invention by routine experimentation by following the teachings provided in the specification. The specification describes methods for expressing and purifying the polypeptides, crystallization and data collection and structure determination and refinement (*see e.g.*, specification at paragraphs [0121-0126] and Table 1). The amino acid sequence and domain characterization of LXRβ LBD are described in the instant application and were known in the art at the time of filing. Detailed structural analysis and predicted location of contact sites was disclosed by Applicants in paragraphs [0089 -0110] of the specification. The three-dimensional coordinates of two representative complexes of LXRβ LBD complexed with T0901317 and GW9365 are also disclosed by the present application. As a result of the present invention, the ligand binding domain of LXRβ was mapped and was shown to include residues Ser242, Phe268, Phe271 , Thr272, Leu274, Ala275, Ser278, Ile309, Met312, Leu13. Glu315, Thr316, Arg319. Ile327, Phe329, Leu330, Tyr335, Phe340. Leu345, Phe349, Ile350, Ile353, Phe354, His435, Gln438, Val1439, Leu442, Leu449, Leu453 and Trp457. Residues important for strong interactions were identified, *e.g.*, His435, and well as residues that can be exploited to develop more potent binding agents (*e.g.*, Phe-271, Thr-272 and Thr-316; see paragraphs [0091-0097] of the specification). Thus, Applicants have disclosed (and optimized) several crystallization conditions of the ligand binding domain of LXRβ. The three-dimensional structures of two of these crystals were disclosed, as well as important residues within the binding pocket.

At the time the instant application was filed, it was known in the art that variants of proteins with known crystallization parameters were likely to readily crystallize with similar crystal structures as long as the variations introduced did not markedly affect intermolecular crystal contacts or amino acids important for protein stability (i.e., within the hydrophobic core). *See* Itoh, S.I. and M.A. Navia (1995) *Protein Science* 4:2261-2268 (copy submitted herewith as Appendix A). Even mutations that had an effect in altering protein stability were found to crystallize with similar crystallization parameters as the native protein. See Sauer, U.H. *et al.* (1992) *Journal of Biological Chemistry* 267:239302399 (copy submitted herewith as Appendix B). Therefore, one of ordinary skill in the art would have been able to practice the claimed

invention, as amended herein, by following the teachings of the specification without undue experimentation.

Applicants respectfully traverse the Office's position with respect to claims 8-10 (currently also including claims 4-5, 7 and 42, as amended herein). These claims are directed to crystals of LXRβ LBD having the space parameters and unit cell dimensions specified. It is submitted that these claims are commensurate in scope with hypothetical claim 1 exemplified in case 4 of the Trilateral Report (discussed above), which was deemed by the USPTO to satisfy the enablement requirement. More specifically, the Trilateral Report states that claims to a crystalline form of a polypeptide (*e.g.*, like claim 1 in case 4 of the Trilateral Report) satisfy the enablement requirement if the specification teaches how to make the claimed crystals and if one skilled in the art could use the claimed polypeptide crystal without undue experimentation (see Trilateral Report, at page 66). As described above, the present specification discloses how to make the claimed invention (*e.g.*, at paragraphs [0121-0126] and Table 1), and one of ordinary skill in the art could have used the claimed crystals without undue experimentation.

The Office Action cites to Branden *et al.*, Drendth *et al.* and others in support of the proposition that the state of the art for making crystals at the time the application was filed unpredictable. Applicants acknowledge that establishing adequate protein crystallization conditions can be a tedious and time-consuming process. In fact the Branden reference cited by the Office describes the availability of automated methods for speeding up "the tedious work of reproducibly setting up a large number of crystallization experiments." *See* Branden *et al.* at page 375.

The fact that some experimentation may be necessary to generate crystals within the scope of the claims does not mandate a conclusion that the experimentation required for such process is necessarily undue as set forth by the CAFC in *Wands*, 858 F.2d 731. As stated in the MPEP §2164.01:

> The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (*Int'l Trade Comm*"*n* 1983) *aff'd. sub. nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104... *See also In re Wands*, 858 F.2d at 737. The test for enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re. Angstadt*, 537 F.2d 498...

The present specification disclosed several crystallization conditions for at least three different complexes of the LXRβ LBD, the amino acid sequence of the LXRβ LBD was disclosed in the specification; at least two three-dimensional structures of the LXRβ LBD were disclosed; as well as residues important for binding activity. Thus, in order to prepare crystals within the space group and/or unit cell parameters disclosed, one of ordinary skill in the art could have simply followed the crystallization conditions disclosed in the specification.

In view of the foregoing, Applicants, therefore, respectfully request reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. § 112, first paragraph, for lack of enablement and written description.

Rejection of Claims 1-6,11,12,29-32 and 35 under 35 U.S.C. § 102(e)

On pages 20-22 of the Office Action, the Office has rejected claims 1-6, 11, 12, 29-32 and 35 under 35 U.S.C. §102(e) as allegedly being anticipated by Bledsoe *et al.* (US Patent Application No. 10/418,007, (effective filing date 04/26/2002)).

Applicants respectfully submit that the pending claims, as amended herein, are novel in view of the Bledsoe priority application (USSN 60/376,019, filed on April 26, 2002). As the presently pending claims are entitled to the priority claimed of December 24, 2002, the arguments below only address the disclosure in USSN 60/376,019.

Bledsoe *et al.* disclose three crystals of a ligand binding domain of human LXRβ consisting of contiguous amino acid residues 214-462, bound to T0901317 belonging to space group $P2_12_12_1$, epoxycholesterol and SRC peptides. The three-dimensional structure disclosed was determined using a truncated monomeric form of human RARγ as a search model.

The Bledsoe priority application fails to anticipate the claims, as presently pending for at least the following reasons:

There is no teaching in the Bledsoe priority application of crystal complexes of GW3965 or TIF2 or space groups $P6_122$, thus claims directed to any of these complexes and space groups are novel in view of this reference (*e.g.*, at least claim 1(b), 2, 6, 10, 29 and 40-42).

Bledsoe priority application discloses a fragment of human LXRβ from amino acid residues 214-462. Claims 1(a), 31 and 31 are directed to crystal forms or human LXRβ

sequences consisting essentially of amino acids 220 to 461 of human LXRβ, which is different from the fragment disclosed in the Bledsoe application.

Remaining claims 4-5, 7-10 and 42 are directed to crystal form of LXRβ LBD having the space group and unit cell parameters specified; none of which is disclosed by the Bledsoe application.

Lastly, claims 29 and 30, as amended herein, are directed to crystallized molecular complexes of the LXRβ LBD having the particular structural coordinates of the binding pocket specified. Moreover, new claim 43 further specifies that the binding pocket was solved by molecular replacements using the structure of the hormone receptor as a search model. Neither of these coordinates, nor search model, is disclosed by Bledsoe *et al.*

In view of the foregoing, reconsideration and withdrawal of this rejection is respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, reconsideration is respectfully requested. This application should now be in condition for allowance; a notice to this effect is respectfully requested. If the Examiner believes, after this amendment, that the application is not in condition for allowance, the Examiner is requested to call the Applicant's attorney at the telephone number listed below.

A petition for a three month extension of time is submitted herewith. Please charge the fee for the three month extension of time and the fee for multiple dependent claims to Deposit Account No. 50/2762. If there is an additional fee occasioned by this response that is not covered by the accompanying authorization, please charge any deficiency to Deposit Account No. 50/2762 referencing Attorney Docket No. W2025-7030US.

Respectfully submitted,
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Docket No.: W2025-7030US
Date: May 30, 2008